Arrowhead Pharmaceuticals Files CTA for Investigational ARO-DIMER-PA – the First Dual Functional RNAi Therapeutic for the Treatment of Mixed Hyperlipidemia

October 7, 2025

- ARO-DIMER-PA is designed to selectively silence the expression of two genes with a single RNAi molecule using Arrowhead's proprietary TRiM ™ technology

- In preclinical studies ARO-DIMER-PA potently lowered serum PCSK9 and APOC3, and ameliorated high levels of non-HDL-cholesterol, LDL-cholesterol, and triglycerides in dyslipidemic nonhuman primates

PASADENA, Calif.--(BUSINESS WIRE)--Oct. 7, 2025-- Arrowhead Pharmaceuticals, Inc. (NASDAQ: ARWR) today announced that it has filed a request for regulatory clearance to initiate a Phase 1/2a clinical trial of ARO-DIMER-PA, the company's investigational RNA interference (RNAi) therapeutic being developed as a potential treatment for atherosclerotic cardiovascular disease (ASCVD) due to mixed hyperlipidemia. ARO-DIMER-PA is designed to silence expression of the proprotein convertase subtilisin kexin 9 (*PCSK9*) and apolipoprotein C3 (*APOC3*) genes. This represents an important step forward for the RNAi field as it is the first clinical candidate to target two genes simultaneously in one molecule, enabled by Arrowhead's innovative and proprietary Targeted RNAi Molecule (TRiM ™) platform.

Mixed hyperlipidemia is a highly prevalent disorder characterized by elevated low-density lipoprotein cholesterol (LDL-C) and triglyceride (TG) levels and is a major risk factor for ASCVD, which is the leading cause of mortality worldwide and associated with substantial morbidity and healthcare costs. Despite the efficacy of LDL-C-lowering therapies in reducing ASCVD risk, there remains substantial residual risk in patients with mixed hyperlipidemia.

"Arrowhead is at the forefront of innovation in the RNAi field and the expansion of the TRiM ™ platform to now include a clinical stage candidate that can potentially silence expression of two genes in one RNAi molecule further reinforces our leadership position. ARO-DIMER-PA silences the *PCSK9* and *APOC3* genes, which both together have substantial clinical validation as important targets for reducing LDL-cholesterol, triglycerides, and total atherogenic lipoproteins. We see this as a promising profile with the potential to reduce the high levels of residual risk of ASCVD that persist," said Chris Anzalone, Ph.D., President and CEO at Arrowhead. "The robust design of our Phase 1/2a clinical study, which is evaluating single and multiple doses directly in patients with mixed hyperlipidemia, may yield important insights into the potential of ARO-DIMER-PA in 2026. With our upcoming November 18, 2025, PDUFA date for plozasiran, which represents our first potential commercial product, and an ongoing Phase 3 for an additional candidate, zodasiran in homozygous familial hypercholesterolemia (HoFH), the addition of ARO-DIMER-PA fits well strategically with our growing commercial focus on RNAi therapeutics in the cardiometabolic therapeutic area."

An application for approval to initiate the clinical trial was submitted to the New Zealand Medicines and Medical Devices Safety Authority for review by the Standing Committee on Therapeutic Trials. Pending clearance, Arrowhead intends to proceed with a Phase 1/2a, randomized, double-blind, placebo-controlled, dose-escalating study to evaluate the safety, tolerability, pharmacokinetics, pharmacodynamics, and effects on LDL-C and TGs of a single-dose of ARO-DIMER-PA (Part 1) and multiple doses of ARO-DIMER-PA (Part 2) in up to 78 adult subjects with mixed hyperlipidemia.

ARO-DIMER-PA is a dual functional RNAi molecule designed to silence expression of the *PCSK9* and *APOC3* genes in hepatocytes. Prior clinical experience with other investigational and approved agents suggests that PCSK9 and APOC3 inhibition may lead to robust reductions in LDL-C, TGs, triglyceride rich lipoprotein remnants, and total atherogenic lipoproteins.

Preclinical data on ARO-DIMER-PA were previously presented at the National Lipid Association (NLA) 2025 Annual Scientific Sessions and may be accessed on the Events and Presentations page under the Investors section of the Arrowhead website.

About Arrowhead Pharmaceuticals

Arrowhead Pharmaceuticals develops medicines that treat intractable diseases by silencing the genes that cause them. Using a broad portfolio of RNA chemistries and efficient modes of delivery, Arrowhead therapies trigger the RNA interference mechanism to induce rapid, deep, and durable knockdown of target genes. RNA interference, or RNAi, is a mechanism present in living cells that inhibits the expression of a specific gene, thereby affecting the production of a specific protein. Arrowhead's RNAi-based therapeutics leverage this natural pathway of gene silencing.

For more information, please visit www.arrowheadpharma.com, or follow us on X (formerly Twitter) at @ArrowheadPharma, LinkedIn, Facebook, and Instagram. To be added to the Company's email list and receive news directly, please visit http://ir.arrowheadpharma.com/email-alerts.

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This news release contains forward-looking statements within the meaning of the "safe harbor" provisions of the Private Securities Litigation Reform Act of 1995. Any statements contained in this release except for historical information may be deemed to be forward-looking statements. Without limiting the generality of the foregoing, words such as "may," "will," "expect," "believe," "anticipate," "hope," "intend," "plan," "project," "could," "estimate," "continue," "target," "forecast" or "continue" or the negative of these words or other variations thereof or comparable terminology are intended to identify such forward-looking statements. In addition, any statements that refer to projections of our future financial performance, trends in our business, expectations for our product pipeline or product candidates, including anticipated regulatory submissions and clinical program results, prospects or benefits of our collaborations with other companies, or other characterizations of future events or circumstances are forward-looking statements. These forward-looking statements include, but are not limited to, statements about the initiation, timing, progress and results of our preclinical studies and clinical trials, and our research and development programs; our expectations regarding the potential benefits of the partnership, licensing and/or collaboration arrangements and other strategic arrangements and transactions we have entered into or may enter into in the future; our beliefs and expectations regarding milestone, royalty or other payments that could be due to or from third parties under existing agreements; and our estimates regarding future revenues, research and development expenses, capital requirements and payments to third parties. These statements are based upon our current expectations and speak only as of the date hereof. Our actual results may differ materially and adversely from those expressed in any forward-looking statements as a result of numerous factors and uncertainties, including the impact of the ongoing COVID-19 pandemic on our business, the safety and efficacy of our product candidates, decisions of regulatory authorities and the timing thereof, the duration and impact of regulatory delays in our clinical programs, our ability to finance our operations, the likelihood and timing of the receipt of future milestone and licensing fees, the future success of our scientific studies, our ability to successfully develop and commercialize drug candidates, the timing for

starting and completing clinical trials, rapid technological change in our markets, the enforcement of our intellectual property rights, and the other risks and uncertainties described in our most recent Annual Report on Form 10-K, subsequent Quarterly Reports on Form 10-Q and other documents filed with the Securities and Exchange Commission from time to time. We assume no obligation to update or revise forward-looking statements to reflect new events or circumstances.

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